

REMARKS

Claims 124-139 and 141-151 are pending. No Amendments have been made. Applicants hereby reserve the right to pursue the claims as originally filed or similar claims in this or one or more subsequent patent applications.

Applicants respectfully note that the Examiner has withdrawn the prior rejections under 35 U.S.C. §102.

Claim Rejections – 35 U.S.C. § 103***Claims 124-139 and 141-150 are rejected under 35 U.S.C. §103(a)***

Claims 124-139 and 141-150 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lee, *et al.* (WO 00/70334) in view of Zee Yong et al. (Anal. Chem. 2001, 73, 2558-2564) and Nelson (US 6,093,541) and Meng et al (Anal Chem 2002, 74, 2923-2929; published on the Web 5/9/2002). Applicants respectfully disagree and traverse the rejection.

It has been asserted in the Office Action, as it has in prior office actions, that: (1) Lee teaches a method of solubilizing a substance using a surfactant of the invention for various spectroscopic techniques; (2) Zee-Yong et al. teach that it is known to denature a protein before digestion before spectroscopic analysis; and (3) Nelson teaches proteases for use in mass spectrometers. The Examiner had previously included Meng which allegedly establishes that it was known in the art to use acid labile surfactants of the instant structure along with sensitivity enhancements for peptide mapping after in-gel digestion.

Applicants have previously argued that nothing in Lee, alone or in combination with Zee Yong, Nelson and Meng, suggests the instantly claimed method. Specifically, that nothing in Lee suggests that the use of the claimed surfactants results in a favorable chemical property in reaction, such as more complete reaction, increased efficiency, increased yield, increased rate, accelerated chemical digestion, or increased utility, as now recited in Claim 124. Nothing in Lee would have lead one of ordinary skill in the art to reasonably expect the enhancement of a chemical digestion using these surfactants. That is to say that Lee, at best, might suggest an increase in solubility of denatured proteins using a surfactant *after the denaturation had already taken place* but would not have suggested an increase in a favorable chemical property of the reaction *during* the denaturation reaction.

The Examiner asserts that as the claim recites that the activity of the protease as claimed is maintained, then the mere solubilization of the protein accounts for the benefits claimed. Similarly, the Examiner argues that nothing of record would teach away from or suggest that the digestion could not be performed in the presence of a surfactant with the reasonable expectation that the protease would function as a protease. Applicants respectfully disagree. Applicants respectfully redirect the Examiner's attention to Example 2 of the instant specification. Specifically, Example 2 / Table 1 shows a trypsin activity assay in which samples treated with SDS as a surfactant were shown to have the activity of the trypsin was **"inhibited activity at each the percentages examined."** Furthermore, the inclusion of the surfactants of the instant invention were able to reactivate the trypsin which had been inhibited by the inclusion of SDS. **This is a surprising and unexpected result.** As such, Applicants respectfully assert that, prior to the instant invention, one of ordinary skill in the art would have had no motivation to expect the maintenance or increase of protease activity upon the inclusion of a surfactant despite the increase in solubility.

Zee-Yong, Nelson and/or Meng do not rectify this deficiency as none of them suggests the use of a surfactant during the denaturation reaction such that the surfactant use results in a favorable chemical property of the alkylation or reduction reaction.

Thus, the prior art does not teach or suggest all of the claim limitations, nor would there be a reasonable expectation of success in achieving the favorable chemical property based only the physical solubilization of the references cited, alone or in combination. Therefore, Applicants submit that the Office Action has failed to establish a *prima facie* case of obviousness.

Applicants submit that the teachings in Lee et al. (WO 00/70334), whether alone or in combination with Zee-Yong et al. and/or Nelson and/or Meng, do not teach or suggest Applicants' claimed subject matter. As such, Applicants respectfully request that the rejections of the claims under 35 U.S.C. § 103(a) should be withdrawn.

Obviousness-Type Double-Patenting

Claims 124-150 are rejected over Claims 1-7, 13-17, and 19 of United States Patent No. 7,229,539. Applicants request that this rejection be held in abeyance until allowance of the instant claims, but for the obviousness-type double-patenting rejection.

CONCLUSION

In view of the amendments and remarks made herein, Applicants submit that the application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. If a telephone conference with Applicants' representative would be helpful in expediting prosecution of the application, Applicants invite the Examiner to contact the undersigned at the telephone number indicated below.

Applicants believe that no additional fees are required in connection with this paper other than the fee for the extension of time submitted herewith. Nevertheless, Applicants authorize the Director to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to Deposit Account No. 04-1105, under Order No. 60009(49991).

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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